

**Notice of Allowability**

Application No.

09/787,215

Examiner

Shaojia A. Jiang

Applicant(s)

KIRCHHOLTES ET AL.

Art Unit

1617

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to February 9, 2005 and May 12, 2005.
2. ☒ The allowed claim(s) is/are 4-6 and 21-29 (now remembered to 1-12).
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

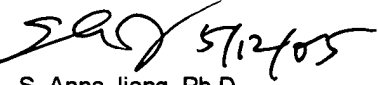
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  6. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date 2/9/05
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

  
S. Anna Jiang, Ph.D.  
Primary Examiner  
Art Unit 1617

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 9, 2005 has been entered.

Applicant's RCE, amendment and response to the Final Office Action (mailed September 9, 2004), filed February 9, 2005 have been entered, wherein claims 4-6 and 21-29 have been amended. Claims 1-3 and 7-20 are cancelled previously.

Currently, claims 4-6 and 21-29 are pending in this application.

### ***Examiner's Amendment***

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

Authorization for this Examiner's Amendment was given in a telephone interview with Mr. Allen C. Turner on May 12, 2004.

The application has been amended as follows:

- Insert the following on page 1 of the instant **specification**, just below the title:

"This application is a 371 of PCT/EP99/07768, filed October 11, 1999, which claims priority to EUROPEAN PATENT OFFICE (EPO) 98203460.5, filed October 16, 1998."

- The **title** has been amended as follows:

"A process for the preparation of a high purity composition comprising (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one"

The **Claims** have been amended as follows:

**Claim 4** (currently amended): A process for reducing the rate of formation of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one impurity in crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one, wherein the (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one contains less than 0.5% by weight of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one as the impurity relative to (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one after drying, said process comprising:

aging crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one in the presence of water for a period of time of at least 24 hours.

**Claim 21.** (Currently amended) The process of claim 4, wherein the process is carried out by comprises:

- (i) washing crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one with water,
- (ii) aging crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one in the presence of water for a period of time of at least 24 hours, and

(iii) drying the

(7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one after at least 24 hours of the washing, wherein the

~~(7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one~~ contains less than 0.5% by weight relative to

~~(7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one~~ as an impurity after drying.

### ***Reasons For Allowance***

Claims 4-6 and 21-29 as amended now are examined on the merits herein.

The claimed process for reducing the rate of formation of the particular impurity, (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one (also known as Org OM38) to less than 0.5 % by weight in the crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one (also known as tibolone) comprising aging crystals of (7 $\alpha$ , 17 $\alpha$ )-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one in the presence of water for a period of time of at least 24 hours, is not seen to be taught or fairly suggested by the prior art, as discussed below.

Applicant's amendment submitted February 9, 2005, in accompanying Examiner's Amendment above, and the disclosed process in Example 2 of the specification herein, and Applicant's remarks regarding the comparative processes of Example 1 and 2, with respect to the rejection of claims 4-6 and 21-29 made under 35 U.S.C. 103(a) as being unpatentable over Sas et al. (EP 389035 A1) and Van Vliet et al. (of record) in the previous Office Action dated September 9, 2004 have been

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considered and found persuasive to remove this rejection, since, first, Sas et al. and Van Vliet et al. do not disclose the particular step in the process, which is aging crystals of tibolone in the presence of water for a period of time of at least 24 hours in order to reduce the impurity Org OM38 to less than 0.5 % by weight.

Second, the comparison of the processes between Example 1 and 2 provided in the response, is deemed to show that the unexpected improvement for reducing the impurity Org OM38 to 0.1 % by weight, by aging crystals of tibolone in the presence of water for 3-6 days was achieved in Example 2, whereas 0.6% by weight of Org OM38 was found in Example 1 without aging the crystals of tibolone in water for at least 24 hours. Note that the process in Example 1 of the specification herein is substantially same as the process taught by Sas et al. (see Example 4 of EP 389035 A1). Hence, the comparative results of the processes between Example 1 and 2 herein is deemed to represent the comparison between the claimed process and the process taught by Sas et al.

Thus, the unexpected results of the claimed process have been considered and found sufficient to rebut the prima facie case of obviousness over the prior art. Therefore, the cited prior art are not deemed to render the instant claimed process obvious to one of ordinary skill in the art. Therefore, the said rejection is withdrawn.

Applicant's amendment filed February 9, 2005 with respect to the rejection of claims 21, 24-25, and 28 made under 35 U.S.C. 112 second paragraph for the insufficient antecedent basis for "tibolone of Org OM38 as an impurity" of record stated in the Office Action dated September 9, 2004 have been fully considered and found

persuasive to remove the rejection since claims 4 and 21 have been amended to remove these indefinite recitations. Therefore, the said rejection is withdrawn.

Accordingly, Applicant's amendment submitted February 15, 2005 in accompanying Examiner's Amendment set forth above are sufficient to remove all rejections made in the prior Office Action as discussed above and place the application in condition for allowance.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner S. A. Jiang whose telephone number is 571.272.0627. The examiner can normally be reached on 9 am -5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.  
Primary Examiner  
Art Unit 1617  
May 12, 2005